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| EXAMINER | |
|---|---|
| KAM, CHIH MIN | |

| ART UNIT | PAPER NUMBER |
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| 1653 | 12 |

DATE MAILED: 07/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. 09/853,193 | Applicant(s) VAN DEN BERGHE, GRETA | |
|---|---|---|---|
| | Examiner Chih-Min Kam | Art Unit 1653 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *09 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *2,3 and 16-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-15 and 19-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8,9* .
4) ☒ Interview Summary (PTO-413) Paper No(s). *12* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

### *Election/Restrictions*

1. Applicant's election with traverse of Group I, claims 1-15 and 19-21, insulin as the blood glucose regulator and critically ill polyneuropathy (CIPNP) as the disease in Paper No. 11 is acknowledged. The traversal is on the ground(s) that each of the listed blood glucose regulators does have a common function (i.e., blood glucose regulation), regardless of their structures, it is the common function is critical to the methods of the invention; regarding to the disease, there is no support for the Examiner's assertion that each disease utilizes different drugs for treatment. The argument is not found persuasive because each type of compounds are structurally different and have different effects in the treatment, thus they are patentably distinct, even they may have the same function, e.g., insulin (a peptide) and sulfonylurea (a small organic compound) are structurally different and have different effects in regulating blood glucose level (The Lancet 352, 837-853 (1998)); regarding the diseases, the diagnosis and the treatment of each disease is different, thus, each disease is patentably distinct from each other, e.g., SIRS can be treated with the antibodies against bacterial endotoxin (Bolton, Crit. Care Med. 24, 1408-1416 (1996)), while stress-induced hyperglycemia can be treated with insulin (McCowen et al., Critical Care Clinics 17, 107-124 (2001). Restriction is proper when two or more claimed inventions are either independent **or** distinct. See MPEP 803. A telephone call was made to Attorney on July 22, 2003 regarding the issue of election of one disease and one type of compound (see attached Interview Summary), applicant indicates he does not dispute each disease is patentably distinct, however, it is not understandable why the election of disease is not a species election. Since each disease and each type of compound is patentably distinct, it would not be treated as a

species election due to the distinct difference among the compounds or diseases. Thus, claims 2 and 3 apparently recite unrelated diseases and are withdrawn from consideration, and claims 1, 4-15 and 19-21, insulin, insulin analogs and insulin derivatives as the blood glucose regulator and critically ill polyneuropathy (CIPNP) as the disease are examined.

The requirement is still deemed proper and is therefore made FINAL.

***Informalities***

The disclosure is objected to because of the following informalities:

2. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (page 10, line 18). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

***Claim Objections***

3. Claims 4-5, 15 and 21 are objected to because the claim contains recitation of non-elected diseases and blood glucose regulators.

4. Claim 20 is objected to because the claim recites "mmole/L)".

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1, 4-15 and 19-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating a critically ill polyneuropathy (CIPNP) patient using insulin as a blood glucose regulator; or treating diabetic cardiac surgery patient with insulin as indicated in the prior art, does not reasonably provide enablement for a

method of treating a critically ill patient, a CIPNP patient or a potential CIPNP patient using a blood glucose regulator, an insulin derivative or an insulin analog, wherein the disease state of the patient and the structure of blood glucose regulator are not defined. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 1, 4-15 and 19-21 encompass a method of treating a critically ill patient, a CIPNP patient or a potential CIPNP patient using a blood glucose regulator (claims 1, 4, 19 and 20), insulin, an insulin derivative or an insulin analog (claim 5-15 and 21). The specification, however, only discloses cursory conclusions without data supporting the findings, which state that the critical illness in a patient or in a CIPNP patient can be treated or prevented by controlling glucose metabolism during the critical illness by applying intensive treatment with a blood glucose regulator such as insulin, active insulin derivatives or other blood glucose regulators (page 3-4). There are no indicia that the present application enables the full scope in view of a method of treating a critically ill patient or a CIPNP patient using a blood glucose regulator as discussed in the stated rejection. The present application provides no indicia and no teaching/guidance as to how the full scope of the claims is enabled. The factors considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the breath of the claims, the absence of working examples, the state of the prior art and relative skill of those in the art, the unpredictability of the art, the nature of the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

(1). The breath of the claims:

The breath of the claims is broad and encompasses unspecified variants regarding the compounds as blood glucose regulators and the diseases in critically ill patient, which are not adequately described or demonstrated in the specification.

(2). The absence or presence of working examples:

There are no working examples indicating the claimed methods in association with the variants except for the treatment of CIPNP with insulin (Examples 1 and 2).

(3). The state of the prior art and relative skill of those in the art:

The prior art (Rassias *et al.*, Anesthsia and Analgesia 88, 1011-1016 (May 1, 1999)) indicates insulin infusion and glucose control during surgery improves white cell function in diabetic cardiac surgery patient. However, the general knowledge and level of the skill in the art do not supplement the omitted description, the specification needs to provide specific teachings on the treating conditions for various diseases in critically ill patients using various blood glucose regulators and the effects of these blood glucose regulators to be considered enabling for variants.

(4). Predictability or unpredictability of the art:

The claims encompass a method of treating a critically ill patient, a CIPNP patient or a potential CIPNP patient using various blood glucose regulators including insulin, insulin derivatives or insulin analogs, however, the treating conditions and the in vivo effects of these various blood glucose regulators are not adequately described in the specification, the invention is highly unpredictable regarding the outcome of the treatment.

(5). The amount of direction or guidance presented and the quantity of experimentation necessary:

The claims are directed to a method of treating a critically ill patient, a CIPNP patient or a potential CIPNP patient using various blood glucose regulators. The specification indicates the CIPNP patient can be treated by controlling glucose metabolism during the critical illness by applying intensive treatment with a blood glucose regulator such as insulin (page 3). However, the specification has not demonstrated the treatment of CIPNP or patients with potential CIPNP or other critical illness using various blood glucose regulators other than insulin used for treating CIPNP. Moreover, there are no working examples indicating the treating conditions such as the dosage, the time for treating CIPNP or other critical illness using various blood glucose regulators with different structures or different glucose-regulating mechanism, nor demonstrating the effects of these blood glucose regulators. Since the specification fails to provide sufficient teachings on the treating conditions for various disease states using various blood glucose regulators, it is necessary to have additional guidance and to carry out further experimentation to assess the effects of these blood glucose regulators in the treatment.

(6). Nature of the Invention

The scope of the claims encompasses a method of treating a critically ill patient, a CIPNP patient or a potential CIPNP patient using various blood glucose regulators, but the specification does not demonstrate the treatment of CIPNP or other critical illness using various blood glucose regulators. Thus, the disclosure is not enabling for the reasons discussed above.

In summary, the scope of the claim is broader than the enabling disclosure. The working examples do not demonstrate the claimed methods, the outcome of the treatment is unpredictable, and the teaching in the specification is limited, therefore, it is necessary to have

additional guidance and to carry out further experimentation to assess the effects of various blood glucose regulators in the treatment of CIPNP or other critical illness.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1, 4-15 and 19-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claims 1, 4-15 and 19-21 are indefinite because the claims lack essential steps in the method of treating critically ill patient or a critically ill polyneuropathy patient. The omitted steps are the effective amount of a blood glucose regulator used and the outcome of the treatment. Claims 5-15, 20 and 21 are included in this rejection for being dependent on a rejected claim and not correcting the deficiency of the claim from which they depend.

8. Claims 1 and 4 are indefinite because of the use of the term "and/or". The term "and/or" renders the claim indefinite, it is unclear whether the limitation after "and/or" is included or not, and if included is to be read as an alternative "or" or the conjunctive "and". Claim 4 is also indefinite because of the term "EMG", it is not clear what the term means.

9. Claim 5 is indefinite because the claim recites being dependent from itself.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10

USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 5 recites the broad recitation "insulin, active insulin derivatives.....and other biologically active substances having insulin releasing action", and the claim also recites "preferably insulin" which is the narrower statement of the range/limitation. Claim 5 is also indefinite because of the term "certain protein-tyrosine phosphatases (PTP's), other type II antidiabetica, and other biologically active substances having insulin releasing action", it is not clear what these compounds are as to "certain" or "other".

10. Claims 9-11 recite the limitation "the blood glucose level" in line 1. There is insufficient antecedent basis for this limitation in the claim.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1, 5, 6, 12, 13 and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Rassias *et al.* (Anesthsia and Analgesia 88, 1011-1016 (May 1, 1999)).

Rassias *et al.* teach the effect of insulin infusion on perioperative neutrophil function in diabetic cardiac surgery patient (claims 12, 13 and 15), and patients (n = 26) were randomized allocated to receive either standard insulin therapy (SIT group) or aggressive insulin therapy (AIT group) during surgery (abstract; page 1011; claims 1 and 5). Protocols of insulin infusion for SIT group and AIT group patients were followed, and the glucose levels were checked before the surgery and then repeatedly intraoperatively using an automated device (page 1022; claim 6). Since claims 1 and 5 do not identify the disease in critically ill patient, the diabetic patients having coronary artery surgery meet the criteria of the claim.

***Conclusions***

12. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (703) 308-9437. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, Ph. D. can be reached on (703) 308-2923. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-0294 for regular communications and (703) 308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

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Patent Examiner

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July 21, 2003